SCIENTIFIC ABSTRACT OF THE STUDY

This gene therapy protocol involves the use of retroviral vector-mediated gene transfer as treatment for human immunodeficiency virus (HIV)-infected individuals. The protocol employs a genetically engineered, non-replicating, amphotropic murine retroviral vector (N2 IIIBenv) encoding the HIV-1 IIIB envelope (ENV and REV) proteins. Preclinical studies have demonstrated the ability of the N2 IIIBenv/rev vector to induce immune responses in mice, Rhesus monkeys, and baboons. Specifically, the N2 IIIBenv/rev vector was capable of inducing HIV-1 IIIBenv/rev-specific $CD8^+$ cytotoxic T lymphocyte (CTL) and antibody responses in these animals. Murine CTL induced by vector transduced cells also exhibited crossreactivity by lysing cells infected with different HIV-1 prototypic strains and clinical isolates. A balanced *in vivo* immune attack by HIV-specific CTL and antibody responses would be expected to eliminate HIV-infected cells and clear cell-free virus, respectively, from an infected individual.

The Phase I/II clinical trial involves the direct administration of the N2 IIIBenv/rev retroviral vector to HIV-infected, seropositive, asymptomatic individuals. The direct vector treatment consists of a series of three monthly intramuscular injections of the test article. The packaging cell line, producer cell line, and processed vector material have undergone extensive quality control analysis for the presence of contaminating agents. Treated individuals will be evaluated for acute toxicity and for routine clinical parameters, CD4 levels, HIV-specific CTL responses, and viral load prior to, during, and following treatment. The treated subjects will also be requested to participate in follow-up for at least three years to identify long-term treatment effects and to evaluate their disease progression.

The study protocol is designed to initially evaluate the safety of the direct administration of retroviral vector-mediated gene therapy as a treatment for individuals with a life-threatening disease. However, functional, biological and clinical disease parameters will be monitored as well to provide a basis for additional human studies.